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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,853	10/02/2003	Nagahide Matsubara	TOYA115.010AUS	5479

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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	**Application No.** 10/677,853	**Applicant(s)** MATSUBARA ET AL.
	Examiner Jeanine A. Goldberg	**Art Unit** 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) *5 and 6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/04; 1/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed December 27, 2005. Currently, claims 1-7 are pending. Claims 5-6 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election of Group I, Claims 1-4, 7 in the paper filed December 27, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Priority

3. This application claims priority to Japanese document 2002-292122, filed October 4, 2002.

It is noted that a translation of the foreign document has not been received.

Drawings

4. The drawings require correction.

Figure 2-3 fails to identify the full nucleotide sequence of a promoter region of a gene encoding hMLH1 by SEQ ID NO: . Appropriate correction is required.

Sequence Rules

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Figure 2-3 fails to identify the full nucleotide sequence of a promoter region of a gene encoding hMLH1 by SEQ ID NO: . Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-4, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al. (US Application 2001/0053519, December 20, 2001).

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Fodor teaches oligonucleotide arrays comprising every 10-mer (less than 100-mer)(limitations of Claim 3, 7). Fodor teaches the regions containing individual probes may be very small, usually less than about 100um x 100um, more usually less than about 50um x50um (para 123)(limitations of Claim 2). Fodor teaches many attachment of nucleotides to solid support mechanisms including the direct attachment of polynucleotides to cellulose by a method involving specific activation of the terminal monosubstituted phosphate or polyphosphate of the polynucleotide by a water soluble carbodiimide (para 78)(limitations of Claim 4).

A 10-mer array would inherently comprises an oligonucleotide sequence complementary to or identical to a nucleotide sequence in which all of C' other than C's in all CpG dinucleotides are replaced with T's and an oligonucleotide sequence complementary to or identical to a nucleotide sequence corresponding to a target sequence in which all of C's are replaced with T's.

7. Claims 1, 3, are rejected under 35 U.S.C. 102(b) as being anticipated by Berlin (WO 01/38565, May 31, 2001) as evidenced by Berlin (US 6,936,419 B1, August 30, 2005).

The WO01/28565 document is in German, therefore the US 371 equivalent is deemed a translation for the WO document.

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Berlin teaches oligomer arrays with PNA and/or DNA oligomers on a surface. Berlin teaches an oligomer array with PNA (peptide nucleic acids) and/or DNA oligomers on a surface, comprising at least 100 different oligomers of between 6 and 20 monomers or nucleobases, whereby at least 75% of said oligomers comprise at least one sequence of the general formula DDCGDD or of the general formula DDTGDD or of the general formula HHCGHH or of the general formula HHCAHH, wherein H indicates one of the bases: adenine (A), cytosine (C), or thymine (T) and D represents one of the bases: adenine (A), guanine (G) or thymine (T), and wherein the site of the oligomers on the surface is correlated with the sequence of the oligomers. The arrays are used for the detection of cytosine methylations in genomic DNA. Berlin teaches the it is preferred that each oligomer, which contains a CG sequence, an analogous oligomer is immobilized, which is distinguished from said [CG] oligomer only by the fact that it contains a TG or a CA instead of the CG sequence (col. 5, lines 1-5). Oligomer arrays are particularly suitable for the detection of cytosine methylations in genomic DNA (col. 5, lines 30-35). Since the sequences on the oligomer array are known, a conclusion on the methylation of the cytosine present on the original DNA is possible (col. 6, lines 60-65).

8. Claims 1-4, 7 are rejected under 35 U.S.C. 102(a) as being anticipated by Suzuki et al. (EPO 1 312 685, May 21, 2003).

A translation of the Japanese foreign has not been provided, therefore, the instant Suzuki publication constitutes a 102(a) type reference. Further, it is noted that the inventors of the instant application and the Suzuki application are not identical.

Suzuki teaches an oligonucleotide array for detecting the methylation state. Suzuki teaches an oligonucleotide-immobilized substrate used for detecting presence or absence of methylation of C in a sample DNA. on which multiple kinds of capture oligonucleotides are immobilized, wherein the sample DNA contains a target sequence containing a dinucleotide consisting of C that can be methylated and a nucleotide on the 3, side of the C (henceforth referred to as "CPN dinucleotide"). The capture oligonucleotides include at least an oligonucleotide having a nucleotide sequence complimentary to or identical to a nucleotide sequence corresponding lo the target sequence in which C's olher than C in the CpN dinucleotide are replaced with T's and an oligonucleotide having a nucleotide sequence complimentary to or identical to a nucleotide sequence corresponding to the target sequence in which all of C's are replaced with T's, and the presence or absence of methylatîon îs detected based on hybridization of the sample DNA in which non- methylated C's have been converted into U's by determination or an amplification product thereof and the capture oligonucleotides. Suzuki teaches the capture probes are immobilized as dots on a base material occupied area of 0.1cm2 or less (page 13)(limitations of Claim 2). The capture probes are oligonucleotides of 30-mer or less (page 13)(limitations of Claim 3, 7).

Suzuki teaches the captures oligonucleotides are immobilized via carbodiimide groups (page 13)(limitations of Claim 4).

9. Claims 1, 3 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Garner et al. (US Publication 2003/0152950 A1, August 14, 2003).

A translation of the Japanese foreign has not been provided, therefore, the instant Garner publication constitutes a 102(a) type reference in addition to a 102(e) type reference.

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Garner teaches identification of chemically modified polymers. As seen in Figure 7, a 190bp region of the p16 promoter region is detailed and each of the CG regions are numbered for analysis (para 22). Garner teaches one set of features was a standard re-sequencing tiling for the sequence expected without methylation (i.e. all Cs converted to T). The other set was a standard re-sequencing tiling for the sequence expected with methylation of every C in each CpG step. The set of probes used in the array appear in Table 1 (para 57).

Garner teaches probe design by analysis of the sequence file. A probe list is created from the complementary sequence and every base is queried. One method for analysis, the first probe starts at position X and extended a number of bases, N. The next probe starts at position X+1 and extends N bases also (para 60). Where multiple CpG islands are on one probe, every possible combination of methylation sites from the parent probe must be created (para 61). For the promoter region of p16, the region contains 36 cytosines, as seen in Figure 7. Each of these cytosines are depicted in Table 2 where 16 cytosines are within CpG dinucleotides and 20 cytosines are not within CpG dinucleotides (para 84). The array was generated using 21 base probes (limitations of Claim 3, 7). Each 21 nucleotide probe is complementary to the sequence surrounding cytosine number 1, with a different base for each probe in apposition to cytosine number 1. As seen in Table 2, each cytosine was queried. Cytosines not part of a CpG were used as an internal standard for unmethyalted position (para 89).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 2, 4, 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berlin (WO 01/38565, May 31, 2001) as evidenced by Berlin (US 6,936,419 B1, August 30, 2005) in view of Fodor et al. (US Application 2001/0053519, December 20, 2001).

The WO01/28565 document is in German, therefore the US 371 equivalent is deemed a translation for the WO document.

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Berlin teaches oligomer arrays with PNA and/or DNA oligomers on a surface. Berlin teaches an oligomer array with PNA (peptide nucleic acids) and/or DNA oligomers on a surface, comprising at least 100 different oligomers of between 6 and 20 monomers or nucleobases, whereby at least 75% of said oligomers comprise at least one sequence of the general formula DDCGDD or of the general formula DDTGDD or of the general formula HHCGHH or of the general formula HHCAHH, wherein H indicates one of the bases: adenine (A), cytosine (C), or thymine (T) and D represents one of the bases: adenine (A), guanine (G) or thymine (T), and wherein the site of the oligomers on the surface is correlated with the sequence of the oligomers. The arrays are used for the detection of cytosine methylations in genomic DNA. Berlin teaches the it is preferred that each oligomer, which contains a CG sequence, an analogous oligomer is immobilized, which is distinguished from said [CG] oligomer only by the fact that it contains a TG or a CA instead of the CG sequence (col. 5, lines 1-5). Oligomer arrays are particularly suitable for the detection of cytosine methylations in genomic DNA (col. 5, lines 30-35). Since the sequences on the oligomer array are known, a conclusion on the methylation of the cytosine present on the original DNA is possible (col. 6, lines 60-65).

Berlin does not specifically teach dot size or means for immobilization.

However, Fodor teaches oligonucleotide arrays. Fodor teaches the regions containing individual probes may be very small, usually less than about 100um x 100um, more usually less than about 50um x50um (para 123)(limitations of Claim 2). Fodor teaches many attachment of nucleotides to solid support mechanisms including the direct attachment of polynucleotides to cellulose by a method involving specific activation of the terminal monosubstituted phosphate or polyphosphate of the polynucleotide by a water soluble carbodiimide (para 78)(limitations of Claim 4).

Therefore, the ordinary artisan would have been motivated to have used very small regions for placing the probe regions of Berlin for the expected results of Fodor. Fordor specifically teaches the very small feature sizes allows very large numbers of probes to be located in very small regions for high throughput screening. The ordinary artisan would have been motivated to have used very small regions for immobilization of probes to facilitate the high density arrays.

Moreover, the ordinary artisan would have been motivated to have immobilize the capture oligonucleotides of Berlin via carbodiimide groups taught by Fodor. Fodor teaches numerous binding immobilization methods including via carbodiimide groups which allows the specific immobilization.

12. Claims 2, 4, 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garner et al. (US Publication 2003/0152950 A1, August 14, 2003) in view of Fodor et al. (US Application 2001/0053519, December 20, 2001).

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Moreover, the ordinary artisan would have been motivated to have immobilize the capture oligonucleotides of Berlin via carbodiimide groups taught by Fodor. Fodor teaches numerous binding immobilization methods including via carbodiimide groups which allows the specific immobilization.

Conclusion

13. No claims allowable over the art.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg
Jeanine Goldberg
Primary Examiner
March 14, 2006